Are 237 published cost-effectiveness models necessary for non-small-cell lung cancer (NSCLC)? Can Open Source "Model Platforms" Improve Decision-Making and Save Resources?

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OBJECTIVES

1. Evaluate the rationale for 237 unique cost-effectiveness models for NSCLC

2. Explore the potential value of an open-source model (OSM) platform in NSCLC

BACKGROUND

Cost-effectiveness models are crucial for allocating limited healthcare resources, particularly for chronic diseases like NSCLC, where the high costs of clinical studies—especially randomized controlled trials—make it challenging to evaluate all relevant comparators and long-term outcomes. As part of I3LUNG (2), a Horizon Europe initiative, we performed a systematic literature review (SLR) of NSCLC cost-effectiveness models, identifying 237 unique models published between 2012 and 2023 (1).

The large number of models is striking, even considering NSCLC's heterogeneity spanning genetic mutations, biomarkers, disease stages, and treatment lines. With a mean quality score of 4.9 of 10 (Figure 1), concerns about reliability arise. The sheer volume of models can also create confusion among stakeholders, especially when results conflict (3, 4), and consume significant resources to develop, validate, and maintain.

OSMs could enhance transparency, quality, and accessibility, reduce duplication, and ease the burden on stakeholders (3-8). Notably, one model identified in the SLR, the Center for Innovation & Value Research (CIVR) NSCLC Value Model, was developed as an OSM (7, 9).

Figure 1. Fulfillment of Modified CHEERS Questions
Source: Willis et al. (1)

METHODS

A. Assessment of Model Heterogeneity and Quality

- Analyzed type of comparison, model type and unit of observation, health states, patient characteristics, mutations considered, intervention, and validation methods
- Each model was evaluated using CHEERS criteria (10), modified by limiting it to 10 model-relevant questions and including an option to assign 0.5 points where incomplete adherence was detected

B. Exploration of OSM Benefits and Challenges in NSCLC

- We reviewed existing literature including one OSM (the CIVR NSCLC Value Model) (7) to outline potential benefits and drawbacks of an OSM platform for NSCLC

RESULTS

A. Heterogeneity Assessment and Model Quality

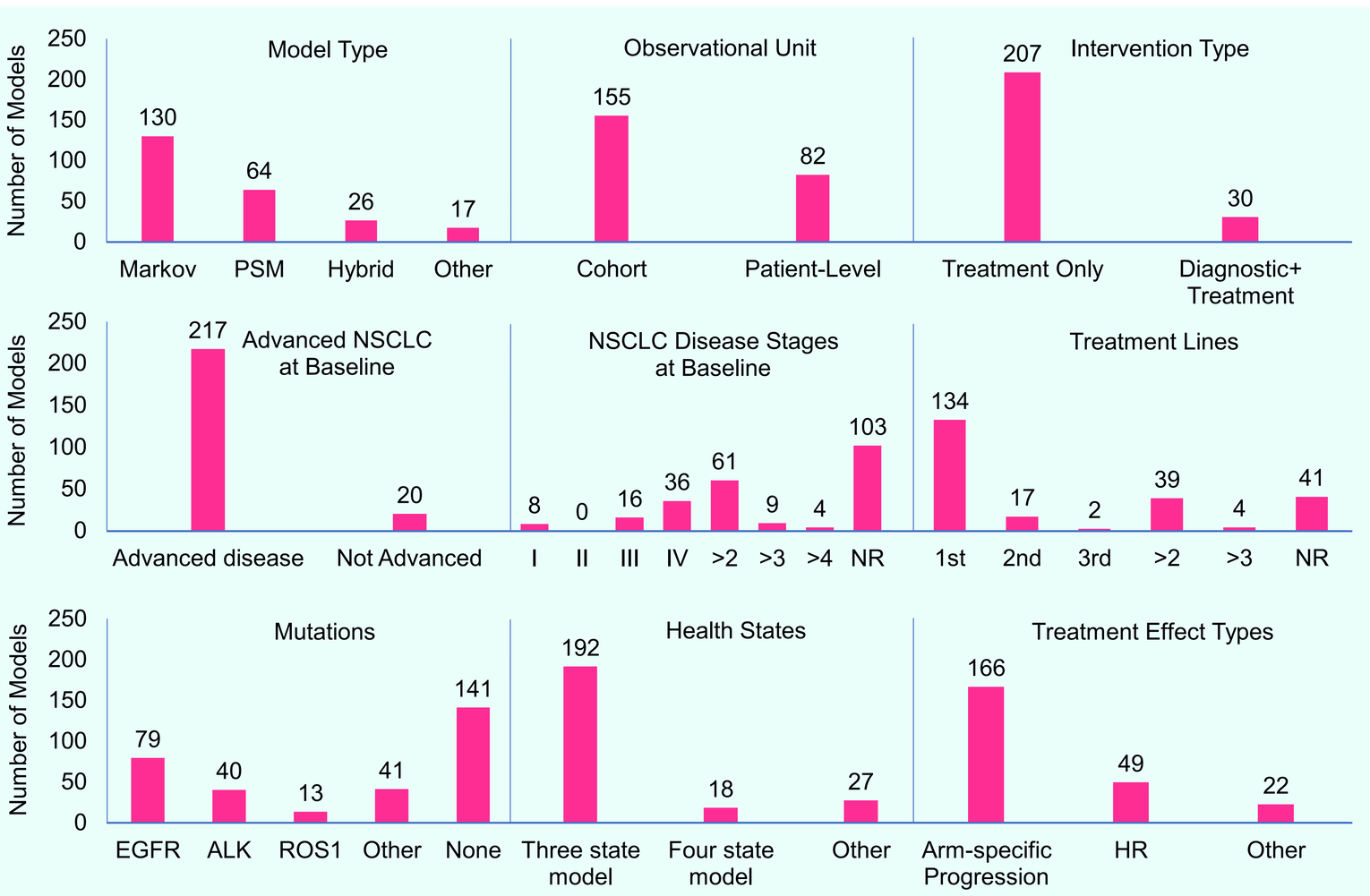

Figure 2. Assessment of Heterogeneity Across Identified Economic Models in NSCLC

- Model structure was homogeneous: 80% used Markov/PSM types, 81% had three health states (progression-free, progressed, dead). Almost half, 45%, combined the three-state and Markov approaches. 70% used event rates that vary by treatment arm (Figure 2)
- Focus areas are also relatively homogenous: 92% support advanced disease; 56% limited to 1st-line treatments
- Differences in handling mutations: 11 different types of mutations were considered in the 40% of models that included mutations. The most common types were EGFR (79 models), ALK (40 models), and ROS1 (13 models). Mutations were more common in models that compared diagnostic technologies (70%) than treatments (36%)
- Only 27% reported any form of validation. Only 4% reported validation results
- Limited adherence to CHEERS: Average score was 4.9, ranging from 2 points to 7.5 points out of 10 (Figure 1)

B. Potential Benefits and Challenges of OSM for NSCLC

- A standardized, validated OSM framework could support healthcare decision-making by (3, 4, 8, 11):
  1. Improving cost-effectiveness estimates, especially as replacements for low-quality models
  2. Boosting decision-maker confidence through reproducibility, reduced stakeholder burden, and enhanced familiarity with model strengths and weaknesses (8)
  3. Improving resource allocation by reducing duplication in model development, validation, and maintenance
- Challenges in NSCLC include:
  1. Funding: proprietary models are still the norm (4, 8, 11), and there is a risk that proprietary model adaptations that deviate from OSM intentions may discourage investment
  2. Flexibility: building models adaptable to the span of possible NSCLC applications can make them complex and less transparent
  3. Sharing source code does not guarantee quality, and multiple versions fragmentation concerns (3, 4)
  4. Sustainability: Success depends on continued modeling community engagement. 237 models suggest a high degree of community interest in NSCLC
- Innovation: Standardizing around one approach risks stifling new solutions.
- An OSM platform for NSCLC is feasible, as shown by the CIVR model (9) for a specific indication. We propose a flexible, open-source platform with:
  1. High-quality, well-documented, modular programming in an accessible language, with full technical documentation (8)
  2. Easy-to-modify model parameters (e.g., transition probabilities, survival curves) and a comprehensive, customizable treatment algorithm including necessary "bells and whistles"
  3. Separate models for different combinations of Markov vs. PSA types and diagnostics vs. treatments, given fundamental differences
  4. Adjustable model features to include all relevant states, perspectives, therapy lines, and diagnostics
  5. Validation of the OSM in line with best practices (12), including verification to ensure correct model implementation and internal and external validation for a broad set of potential applications. Note, the OSM must be re-validated to the specific setting it has been customized to

DISCUSSION

- Open-source models (OSMs) are recognized for transparency and resource efficiency. The structural homogeneity and limited quality of NSCLC models suggests potential for gains from well-designed open-source options. A recent public-feedback-driven model provides proof of concept in NSCLC (7)
- While the 237 NSCLC models may be an outlier, similarities across cancer models suggest broader applicability for OSMs in oncology, as in Alzheimer's disease (5) and rheumatoid arthritis (13)
- There are many challenges, including technical, legal, and data-sharing barriers (3, 8). In fact, it is unclear who might develop, validate, and continuously improve open-source models, but more stakeholder demand for open-source models could help provide an impetus
- This is a theoretical exercise, and our intention is not to suggest the use of only model; fit-for-purpose proprietary models will always play a role
- As part of I3LUNG, we are currently developing an open-source Markov model for assessing diagnostic technologies, one of the four model types proposed

CONCLUSIONS

Redundancy and quality concern in 237 existing NSCLC models highlight the potential value that could be created by an OSM

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